General

Guideline Title

ACR Appropriateness Criteria® chronic chest pain—high probability of coronary artery disease.

Bibliographic Source(s)

Akers SR, Panchal V, Ho VB, Beache GM, Brown RK, Ghoshhajra BB, Greenberg SB, Hsu JY, Kicska GA, Min JK, Stillman AE, Stojanovska J, Abbara S, Jacobs JE, Expert Panel on Cardiac Imaging. ACR Appropriateness CriteriaÂ® chronic chest painâ€"high probability of coronary artery disease. Reston (VA): American College of Radiology (ACR); 2016. 12 p. [99 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Earls JP, White RD, Woodard PK, Abbara S, Atalay MK, Carr JJ, Haramati LB, Hendel RC, Ho VB, Hoffman U, Khan AR, Mammen L, Martin ET III, Rozenshtein A, Ryan T, Schoepf J, Steiner RM, White CS, Expert Panel on Cardiac Imaging. ACR Appropriateness Criteria chronic chest pain -- high probability of coronary artery disease. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 9 p. [70 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Chronic Chest Pain—High Probability of Coronary Artery Disease

Variant 1: Chronic chest pain; high probability of coronary artery disease.

Radiologic Procedure	Rating	Comments	RRL*
X-ray chest	9		☢
Tc-99m SPECT MPI rest and stress	9		☢☢☢☢
MRI heart with function and vasodilator stress perfusion without and with IV contrast	9		O

Radiologic Procedure	Rating	Comments	RRL*
Arteriography coronary	9		☢☢☢
Rb-82 PET heart stress	8		☢☢☢
US echocardiography transthoracic stress	8		O
CTA coronary arteries with IV contrast	8		☢☢☢
MRI heart with function and inotropic stress without and with IV contrast	7		O
MRI heart with function and inotropic stress without IV contrast	7		O
MRI heart function and morphology without and with IV contrast	7		O
MRA coronary arteries without and with IV contrast	5		O
US echocardiography transthoracic resting	4		O
MRI heart function and morphology without IV contrast	4		O
MRA coronary arteries without IV contrast	4		O
CT chest with IV contrast	4		☢☢☢
CT chest without IV contrast	4		☢☢☢
CT chest without and with IV contrast	4		☢☢☢
US abdomen	3		O
CT coronary calcium	3		☢☢☢
TC-99m ventriculography	3		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Chronic chest pain of suspected cardiac origin is usually a consequence of myocardial ischemia, representing an imbalance between myocardial oxygen demand and coronary blood flow. This is usually caused by fixed, hemodynamically significant coronary stenosis due to atherosclerotic plaque formation leading to reduced myocardial perfusion. Less common causes of chronic chest pain include coronary spasm, microvascular disease, or a combination of both. In the setting of high probability of coronary artery disease (CAD), flow-limiting epicardial coronary artery narrowing is most likely. However, chest pain of myocardial ischemic origin can also occur in patients with relatively normal coronary arterial caliber but with conditions resulting in increased demand for oxygenation (e.g., increased myocardial mass and workload due to systemic arterial hypertension or aortic stenosis). Although the syndrome of exertional angina pectoris is nearly always diagnostic of chronic CAD, nonischemic cardiac (e.g., myocarditis, pericarditis) and extracardiac (e.g., esophageal reflux/spasm) etiologies and costochondritis should also be considered in the setting of nonexertional or atypical chest pain.

In patients with chronic chest pain in the setting of high probability of CAD, imaging has major and diverse roles. First, imaging is valuable in determining and documenting the presence, extent, and

severity of myocardial ischemia, hibernation, scarring, and/or the presence, site, and severity of obstructive coronary lesions. Second, imaging findings are important in determining the course of management of patients with suspected chronic myocardial ischemia and better defining those patients best suited for medical therapy, angioplasty/stenting, or surgery. Third, imaging is also necessary to determine the long-term prognosis and likely benefit from various therapeutic options by evaluating ventricular function, diastolic relaxation, and end-systolic volume. Imaging studies are also required to demonstrate abnormalities (e.g., congenital or acquired coronary anomalies, severe left ventricular [LV] hypertrophy) that can produce angina in the absence of symptomatic coronary obstructive disease due to atherosclerosis.

Clinical risk assessment is necessary to determine the pretest probability of CAD. Multiple methods are available to categorize patients as low, medium, or high risk of developing CAD. Existing methods, including the Diamond and Forrester method, Framingham risk score, coronary calcium score (CCS), and Duke Clinical Score, are based on different criteria such as age, gender, family history of CAD, type of chest pain, lipid levels, and previous cardiovascular events. One study suggests that the Diamond and Forrester method overestimates the prevalence of obstructive CAD and the Duke Clinical Score performs better in low-risk patients. One research group suggested that stable CAD would be more accurately risk stratified using the CCS rather than the Diamond and Forrester method. In conclusion, risk assessment for CAD using various existing methods can lead to variable pretest probability and may stratify patients in different risk categories.

The imaging modalities historically used in evaluating suspected chronic myocardial ischemia are: 1) chest radiography; 2) stress and rest radionuclide single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI); 3) catheter-based selective coronary angiography with or without left ventriculography; and 4) radionuclide ventriculography (RVG) with and without stress. Stress echocardiography, positron emission tomography (PET), cardiac magnetic resonance imaging (MRI), and multidetector cardiac CT (MDCT) have all been more recently shown to be valuable in the evaluation of ischemic heart disease. In those patients who do not present with signs classic for angina pectoris, or in those patients who do not respond as expected to standard management, the exclusion of noncardiac causes of chronic chest pain requires the use of additional studies (e.g., esophagography, upper gastrointestinal series, and biliary ultrasound [US]).

Chest Radiography

The chest radiograph is an inexpensive test that can rapidly demonstrate many noncardiac causes of chronic chest pain, including a variety of diseases of the mediastinum, pleura, or lung. It may also provide qualitative indirect information about LV function as reflected in cardiac size and pulmonary vascular patterns (e.g., pulmonary venous hypertension). However, chest radiographs can neither establish nor exclude chronic ischemic heart disease. In addition, radiographs (including fluoroscopy) are insensitive for detecting coronary arterial calcification. Chest radiography, therefore, is of limited value in symptomatic patients with high risk of CAD.

Imaging of Myocardium

Single Photon Emission Computed Tomography

Stress SPECT MPI demonstrates relative myocardial perfusion defects, indicating the presence of myocardial ischemia. For this reason, it is considered an important first-line study in the evaluation of patients with chronic chest pain and a high likelihood of CAD. By acquiring rest and stress perfusion scans, it is possible to demonstrate reversibility (ischemia) or irreversibility (infarction) of a myocardial perfusion defect. The territory of the perfusion defect identifies the likely culprit coronary artery and can distinguish between significant single-vessel and multi-vessel coronary arterial obstructions. The magnitude of the abnormality and the presence of high-risk findings also assist in clinical decision making.

Presently, SPECT perfusion agents labeled with technetium 99^{m} (Tc-99m), such as Tc-99m sestamibi or Tc-99m tetrofosmin, are used most commonly because of improved image resolution, higher count

density, and more favorable dosimetry. The sensitivity and specificity for Tc-99m–agent SPECT in detecting CAD are equal to and usually superior to those of thallium-201 (^{201}Tl). With the use of electrocardiogram (ECG) gating, and with improved imaging protocols and image quality, the diagnostic accuracy of stress SPECT MPI for detecting angiographically significant CAD is high (sensitivity 87% to 89% and specificity 73% to 75%). More importantly, a normal stress SPECT MPI examination in patients with intermediate to high likelihood of CAD predicts a very low rate of cardiac death or nonfatal myocardial infarction (MI) (≤1% per year). Furthermore, SPECT MPI may be used for risk stratification in scenarios such as follow-up after percutaneous coronary intervention and coronary artery by-pass graft (CABG), or evaluation prior to noncardiac surgery. Limitations of stress SPECT MPI are its relatively high cost and relatively high radiation dose.

Software algorithms such as iterative reconstruction, maximum a posteriori noise regularization and resolution-recovery, and new hardware and detector materials continue to be refined, allowing for image acquisitions at significantly shorter acquisition times or, alternatively, at lower doses of radiation compared to conventional algorithms.

Stress radionuclide ventriculography consists of measurement of the ejection fraction and assessment of regional wall motion at rest and during stress. However, radionuclide ventriculography is rarely used as SPECT MPI has largely replaced it; hence availability of and expertise with this method are very limited. In patients with typical angina (high pretest likelihood of disease), stress SPECT MPI is useful for estimating the extent (single-vessel versus multivessel disease) and severity of coronary stenosis, which has relevance for prognosis, choice among therapeutic options, and advisability of performing coronary arteriography.

Hybrid SPECT/coronary computed tomography angiography (CCTA) combines the anatomical information provided by computed tomography (CT) with the functional perfusion evidence of SPECT, resulting in enhanced diagnostic accuracy for detecting significant CAD compared to SPECT and CCTA alone. One study found that the sensitivity and specificity of hybrid SPECT/CCTA were 96% and 95%, respectively, compared with SPECT (93% and 79%) and CCTA (98% and 62%) alone. There was 92% agreement on the necessity of revascularization in the treatment decisions based on hybrid SPECT/CCTA versus SPECT and coronary angiography alone. Thus, the combination of SPECT and CCTA provides excellent diagnostic performance and compensates for the drawbacks of each technique as a stand-alone imaging procedure.

Positron Emission Tomography

Myocardial PET imaging using rubidium-82 (^{82}Rb) or nitrogen N-13 ammonia for assessing perfusion, and fluorine-18-2-fluoro-2-deoxy-D-glucose for evaluating metabolism, are now recognized as useful methods for the evaluation of ischemic heart disease. PET perfusion imaging has several advantages over SPECT, including higher spatial and temporal resolution, superior attenuation and scatter correction, and the capability to perform quantitative measurements. In a meta-analysis of 8 studies with 791 patients evaluated for CAD by PET perfusion imaging, the overall sensitivity and specificity were determined to be 93% and 92%, respectively. In the same article, 3 studies comparing ^{201}Tl SPECT with ^{82}Rb or N-13 ammonia PET were analyzed, and the overall accuracy of PET was 91%, compared with 81% for ^{201}Tl SPECT. Gated PET also provides assessment of LV function and overall provides important diagnostic and prognostic data.

Hybrid PET scanners use CT for attenuation correction (PET/CT) following completion of the PET study. By coupling the PET perfusion examination findings to a CCTA, PET/CT permits the fusion of anatomic coronary arterial and functional (perfusion) myocardial information and enhances diagnostic accuracy. The fused examinations can accurately measure the atherosclerotic burden and identify the hemodynamic functional significance of coronary stenoses. The results of the combined examinations can more accurately identify patients for revascularization. In a study of 110 consecutive patients with combined stress ^{82}Rb PET perfusion imaging and CCTA, nearly half of significant angiographic stenoses (47%) occurred without evidence of ischemia, whereas 50% of normal PET studies were associated with some CCTA abnormality.

Echocardiography

Stress 2-dimensional (2-D) echocardiography for myocardial contractility assessment is increasingly used for patients with suspected regional wall motion abnormalities secondary to regional ischemia, in part because of the ubiquity of 2-D echocardiography. In patients for whom exercise is not feasible, pharmacologic stress echocardiography is performed. A meta-analysis of 44 studies indicated that stress echocardiography has a similar sensitivity to stress SPECT MPI (85% and 87%, respectively), with a higher specificity (77% vs 64%). A study that compared dobutamine-atropine stress echocardiography and dipyridamole Tc-99m sestamibi SPECT found that SPECT had similar sensitivity for detection of CAD, with dobutamine-atropine stress echocardiography being more specific (91% versus 73%). A different study also showed that dobutamine stress echocardiography and perfusion scintigraphy have equivalent accuracy for diagnosing obstructive CAD. Stress echocardiography includes rest as well as stress images.

In a meta-analysis of 435 patients, dipyridamole and dobutamine stress contractility echocardiography had similar accuracy (87% versus 84%), specificity (89% versus 86%), and sensitivity (85% versus 86%) for detecting CAD. The pharmacologic stress echocardiography techniques are limited by the fact that they sometimes yield nondiagnostic results and that suboptimal definition of some regions of the LV can lead to subjective interpretation.

Administration of an echocardiography contrast agent (i.e., microbubbles) improves endocardial visualization at rest and more so during stress, leading to a more precise interpretation with greater accuracy in evaluating CAD in patients with 2 or more nonvisualized segments and low confidence of interpretation.

Rest transthoracic echocardiography (TTE) can be useful if pericardial effusion or valvular or chamber abnormalities are suspected. Transesophageal echocardiography is generally not indicated for evaluating chronic angina and the feasibility of this study does not justify its use in this setting. However, it is sometimes used for assessing aortic pathology (e.g., dissection, aneurysm, and penetrating ulcer) in patients with chronic chest pain, although CT and MRI are less invasive and simpler to perform.

Magnetic Resonance Imaging

Use of MRI for evaluating general cardiac anatomy and function and specific aspects of valvular disease, cardiomyopathies, myocardial viability, is well established.

MRI myocardial perfusion techniques can be used to assess for significant CAD. The diagnostic accuracy of stress perfusion MRI has been evaluated by many studies and has been found to be equivalent, and in many cases superior, to stress SPECT MPI. The CE-MARC trial, the largest prospective evaluation of MRI, revealed that MRI and SPECT had similar specificity and positive predictive value (PPV), with the sensitivity and negative predictive values (NPV) of MRI significantly better than SPECT (sensitivity, 86.5% versus 66.5%; NPV, 90.5% versus 79.1%). A meta-analysis from pooled studies found that perfusion stress MRI has a sensitivity of 89.1% and a specificity of 84.9% on a patient-based analysis using fractional flow reserve (FFR) as a reference, suggesting that stress perfusion MRI remains an accurate test for the detection of flow-limiting stenosis. One study reported that MRI is highly sensitive for the detection of CAD with moderate specificity. Another study concluded that MRI perfusion diagnoses CAD better than echocardiography and SPECT.

Clinically, MRI with function and vasodilator stress perfusion has been used to diagnose hemodynamically significant CAD in patients with intermediate to high likelihood of having significant stenosis. The technique is commonly used in patients with poor acoustic windows in whom stress echocardiography imaging would be difficult to visualize. It has also been shown to have a higher diagnostic accuracy than dobutamine stress echocardiography. In patients with poor echocardiography examinations, dobutamine stress MRI can be used to predict myocardial infarction or cardiac death.

Despite its superior diagnostic performance, MRI is generally not appropriate for evaluating the individual chronic chest pain patient with a high probability of CAD in the setting of implanted electronic devices (e.g., permanent pacemaker, an implantable cardioverter defibrillator). In addition, general reliance on MRI in assessing chronic chest pain is hindered by the limited availability of advanced facilities and

experienced personnel.

Imaging of Coronary Arteries

Computed Tomography

MDCT as well as electron-beam CT (less commonly used) are used for detecting the presence and severity of calcification, a sign of coronary atherosclerosis. In a large study of 10,377 patients, the authors showed that CCS provides independent incremental information in the prediction of all-cause mortality.

In a prospective study, another group found that even in patients with a CCS of 0, there was a 4.3% prevalence of CAD. Thus, a CCS of 0 does not reliably exclude obstructive CAD among patients with a high suspicion of CAD. On the other hand, patients who do present with chronic chest pain of suspected cardiac origin are typically older, with a significant proportion older than 60 years of age. Because coronary calcium is so prevalent in this population, a "positive" CCS, even in the upper quartiles, cannot be used as strong evidence of myocardial ischemia.

CCTA uses iodinated contrast and ECG-gated MDCT to evaluate for CAD. Studies using 64-slice CCTA have shown a high sensitivity and high NPV for treatable stenoses of the coronary arteries. A recent meta-analysis to evaluate the diagnostic accuracy of 64-slice CCTA compared with conventional selective coronary angiography included 27 studies and 1740 patients and found that the sensitivity, specificity, PPV, and NPV were 86%, 96%, 83%, and 96.5%, respectively, by per-segment analysis and 97.5%, 91%, 93%, and 96.5%, respectively, by per-patient analysis. The CCTA ACCURACY trial found 95% sensitivity, 83% specificity, 64% PPV, and 99% NPV for detection of CAD, suggesting that CCTA possesses high diagnostic accuracy for detecting coronary stenosis at thresholds of 50%. The high NPV (99%) also establishes CCTA as an effective noninvasive alternative to invasive coronary angiography (ICA) to exclude CAD in low-risk patients.

However, the pretest probability of CAD does impact the diagnostic performance of CCTA in high-risk patients, the population under consideration in this document. In CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography), the pretest probability and CCS significantly affect NPV for detecting obstructive CAD by CCTA. Therefore, both pretest probability for CAD and coronary artery calcium scoring should be considered before using CCTA for excluding obstructive CAD. The NPV of CCTA is significantly lower in patients with a high prevalence of CAD, and a negative CCTA reduces the estimated posttest probability of having obstructive disease only to approximately 17%. Because of this high residual post-test probability despite a negative CCTA, many symptomatic high-probability patients are likely to still require invasive selective coronary angiography. CCTA, therefore, may be of limited clinical value in the evaluation of the high-estimated-pretest-probability group.

There are 2 additional special considerations for CCTA. The first is a stress perfusion CT that can be performed as an additional data acquisition, but during the same imaging session as CCTA. CT myocardial perfusion adds a functional estimate of myocardial perfusion to the CCTA data, using iodinated contrast as a perfusion agent. CT perfusion improves the diagnostic value for detecting CAD compared to CCA alone, particularly in patients with severe calcification. CT perfusion imaging was shown when combined with CTA to accurately predict atherosclerotic perfusion abnormalities when compared with coronary angiography and SPECT. In addition, CT perfusion was demonstrated to be highly accurate in determining the presence or absence of myocardial ischemia in patients with obstructive CAD when compared with SPECT MPI in the presence of stenosis (≥50% of CTA) with a sensitivity, specificity, PPV, and NPV of 100%, 81%, 50%, and 100%, respectively, and an area under the curve of 0.92.

The second special consideration is the emergence of methods applied to CCTA data after image acquisition to estimate FFR. For example, the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) concluded that FFR estimates from postprocessed CT images provide high diagnostic accuracy for the diagnosis of hemodynamically significant CAD with ICA as a reference. Other studies have supported this emerging technology. Neither CT perfusion (where separate data are acquired in addition to the CCTA) nor FFR estimates (image analysis steps applied to CCTA images) were

independently considered in the panel ratings.

Magnetic Resonance Angiography

Although MR angiography (MRA) of the pulmonary and systemic vessels has matured significantly in the last decade, MRA of the coronary arteries is still problematic because of their small size and incessant motion tied to the respiratory and cardiac cycles. At this time, coronary MRA should be limited to sites with extensive experience and appropriate capabilities to exclude disease in the proximal coronary arteries. At present, only CCTA can noninvasively visualize coronary arteries on a routine basis; in direct comparison, coronary MRA had similar sensitivity but significantly lower specificity and accuracy as compared with CCTA.

Selective Coronary Angiography

Catheter-based selective coronary angiography remains the coronary imaging modality of choice with the highest spatial and temporal resolution. Although only projection images are obtained (as opposed to 3-D volumes in CCTA), selective coronary angiography is considered to be the gold standard for depicting the anatomy and the severity of obstructive CAD and some other coronary arterial abnormalities (e.g., coronary spasm). In addition to visualizing the coronary arteries, the procedure is used to guide stents to the site of blockage.

FFR measurement accurately estimates the functional severity of stenosis in obstructive CAD. In the FAME 2 trial (Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2), the authors concluded that performing FFR in addition to PCI resulted in a lower end-point composite death rate at 1 year (13.2% versus 18.3%) compared with performing PCI alone. FAME 2 trial findings suggest that in patients with stable CAD with functionally significant stenosis, FFR-guided PCI with optimal medical therapy reduced revascularization rates (1.6% versus 11.1%) compared with optimal medical therapy alone. Thus, FFR has been validated to be an essential component of ICA to diagnose CAD.

There is conclusive evidence that selective coronary angiography is indicated in patients in whom angina is not adequately managed by aggressive medical therapy and in those in whom left coronary artery stenosis or severe multivessel CAD is suggested by results of stress SPECT MPI or stress echocardiography or CCTA.

LV catheterization and left ventriculography are generally indicated, but not always necessary, to define ventricular function in patients with angina. Currently, noninvasive imaging techniques like MRI and echocardiography are used more frequently to define LV function.

Other noncardiac diagnostic studies, such as abdominal US and chest CT, should be considered only after a cardiac etiology has been accurately excluded using the appropriate imaging modalities and clinical evaluation described above.

Summary of Recommendations

> The chest radiograph is a good initial assessment of the overall thorax in a patient with chronic chest pain.
> Coronary angiography is the current gold standard for evaluating CAD, allowing immediate intervention, although it is an invasive procedure with associated risks.
> CTA of the coronary arteries provides not only coronary artery stenosis evaluation similar to that of catheterization but plaque analysis as well as morphologic and, if desired, functional information.
> Stress MRI, SPECT MPI, PET, and TTE are first-line modalities in noninvasively identifying ischemia and indirectly assessing CAD. In addition, these procedures provide functional and morphologic cardiac information.

Abbreviations

> CT, computed tomography
> CTA, computed tomography angiography
> IV, intravenous

MDCT, multidetector computed tomography
MPI, myocardial perfusion imaging
MRA, magnetic resonance angiography
MRI, magnetic resonance imaging
PET, positron emission tomography
Rb, rubidium
SPECT, single-photon emission computed tomography
Tc-99m, technetium-99 metastable
US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Chronic chest pain with high probability of coronary artery disease (CAD)

Guideline Category

Diagnosis

Evaluation

Risk Assessment

Clinical Specialty

Cardiology

Emergency Medicine

Family Practice

Internal Medicine

Nuclear Medicine

Radiology

Intended Users

Advanced Practice Nurses

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging procedures for patients with chronic chest pain with high probability of coronary artery disease (CAD)

Target Population

Patients with chronic chest pain with high probability of coronary artery disease (CAD)

Interventions and Practices Considered

1. X-ray, chest
2. Technetium (Tc)-99m single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), rest and stress
3. Magnetic resonance imaging (MRI), heart
    - With function and vasodilator stress perfusion without and with intravenous (IV) contrast
    - With function and inotropic stress without and with IV contrast
    - With function and inotropic stress without IV contrast
    - Function and morphology without and with IV contrast
    - Function and morphology without IV contrast
4. Rubidium (Rb)-82 positron emission tomography (PET), heart, stress
5. Coronary arteriography
6. Ultrasound (US)
    - Echocardiography, transthoracic stress
    - Echocardiography, transthoracic resting
    - Abdomen
7. Computed tomography angiography (CTA), coronary arteries with IV contrast
8. Magnetic resonance angiography (MRA), coronary arteries
    - Without and with IV contrast
    - Without IV contrast
9. Computed tomography (CT)

    - Chest with IV contrast
    - Chest without IV contrast
    - Chest without and with IV contrast
    - Coronary calcium
10. Technetium-99 metastable (Tc-99m) ventriculography

Major Outcomes Considered

- Utility of imaging modalities in diagnosing and evaluating chronic chest pain with high probability of coronary artery disease (CAD)
- Sensitivity, specificity, and diagnostic accuracy of imaging modalities in evaluating chronic chest pain with high probability of CAD

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 70 citations in the original bibliography, 54 were retained in the final document.

A literature search was conducted in August 2012, November 2013, January 2015, and June 2015 to identify additional evidence published since the *ACR Appropriateness Criteria® Chronic Chest Pain—High Probability of Coronary Artery Disease* topic was finalized. Using the search strategies described in the literature search companion (see the "Availability of Companion Documents" field), 672 articles were found. Thirty articles were added to the bibliography. Ninety-five articles were not used as they were duplicates already cited in the original bibliography or captured in more than one literature search. The remaining articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, or the results were unclear or biased.

The author added 15 citations from bibliographies, Web sites, or books that were not found in the literature searches.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 70 citations in the original bibliography, 54 were retained in the final document. The literature search conducted in August 2012, November 2013, January 2015, and June 2015 identified 30 articles that were added to the bibliography. The author added 15 citations from bibliographies, Web sites, or books that were not found in the literature searches.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness. When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the first rating round, a conference call is scheduled to discuss the evidence and, if needed, clarify the variant or procedure description. If there is disagreement after the second rating round, the recommendation is "May be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 99 references cited in the *ACR Appropriateness Criteria® Chronic Chest Pain—High Probability of Coronary Artery Disease* document, 84 are categorized as diagnostic references, including 8 well-designed studies, 36 good-quality studies, and 29 quality studies that may have design limitations. Additionally, 5 references are categorized as therapeutic references, including 4 well-designed studies. There are 12 references that may not be useful as primary evidence. There are 10 references that are meta-analysis studies.

Although there are references that report on studies with design limitations, 48 well-designed or good-quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

In patients with chronic chest pain in the setting of high probability of coronary artery disease (CAD), imaging has major and diverse roles. First, imaging is valuable in determining and documenting the presence, extent, and severity of myocardial ischemia, hibernation, scarring, and/or the presence, site, and severity of obstructive coronary lesions. Second, imaging findings are important in determining the course of management of patients with suspected chronic myocardial ischemia and better defining those patients best suited for medical therapy, angioplasty/stenting, or surgery. Third, imaging is also necessary to determine the long-term prognosis and likely benefit from various therapeutic options by evaluating ventricular function, diastolic relaxation, and end-systolic volume. Imaging studies are also required to demonstrate abnormalities (e.g., congenital or acquired coronary anomalies, severe left ventricular [LV] hypertrophy) that can produce angina in the absence of symptomatic coronary obstructive disease due to atherosclerosis.

Potential Harms

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ

sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply society endorsement of the final document.
- The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or reflecting the views of the Uniformed Services University of the Health Sciences or the Department of Defense.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Identifying Information and Availability

Bibliographic Source(s)

Akers SR, Panchal V, Ho VB, Beache GM, Brown RK, Ghoshhajra BB, Greenberg SB, Hsu JY, Kicska GA, Min JK, Stillman AE, Stojanovska J, Abbara S, Jacobs JE, Expert Panel on Cardiac Imaging. ACR Appropriateness CriteriaÂ® chronic chest painâ€"high probability of coronary artery disease. Reston (VA): American College of Radiology (ACR); 2016. 12 p. [99 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

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American College of Radiology - Medical Specialty Society

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Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Cardiac Imaging

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Earls JP, White RD, Woodard PK, Abbara S, Atalay MK, Carr JJ, Haramati LB, Hendel RC, Ho VB, Hoffman U, Khan AR, Mammen L, Martin ET III, Rozenshtein A, Ryan T, Schoepf J, Steiner RM, White CS, Expert Panel on Cardiac Imaging. ACR Appropriateness Criteria chronic chest pain -- high probability of coronary artery disease. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 9 p. [70 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site .

ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2016. 4 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2016. 128 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2016 May. 2 p. Available from the ACR Web site .

ACR Appropriateness Criteria® chronic chest pain—high probability of coronary artery disease. Evidence table. Reston (VA): American College of Radiology; 2016. 49 p. Available from the ACR Web site .

ACR Appropriateness Criteria® chronic chest pain—high probability of coronary artery disease. Literature search. Reston (VA): American College of Radiology; 2016. 2 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

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